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Illness Following MMR Immunization In Indian and Non-Indian Children

SUMMARY

A cohort study was undertaken to see if the frequency of office reported illness during the three weeks after MMR immunization was greater among Indian children (N=127) compared to non-Indian children (N=81) attending a family practice centre. All children had been given $HPV_{77}DE_5$ vaccine or RA 27/3 vaccine between ages 11 and 24 months. Illness after immunization was not related to frequency of attendance at the medical centre or weight at age 12 months. The overall illness rate for Indian children was almost twice the rate for non-Indians. Indian children who were ill before immunization were more likely to be ill during the three week post-MMR period. No such relationship was noted among non-Indian children. This suggests that children with an established record of frequent illness are likely to experience an illness following MMR immunization. These results need to be confirmed by a prospective study. (Can Fam Physician 1983; 29:1445-1450).

SOMMAIRE

Une étude cohorte a été entreprise afin de déterminer si la fréquence de maladie au cours des trois semaines suivant l'immunisation MMR était plus grande chez les enfants indiens (N=127) comparativement aux enfants non-indiens (N=81) suivis dans une clinique familiale. Tous les enfants ont reçu le vaccin $HPV_{77}DE_5$ ou le vaccin RA 27/3 entre les âges de 11 et 24 mois. La maladie après immunisation n'était pas reliée à la fréquence des visites à la clinique médicale ou au poids à l'âge de 12 mois. Le taux de maladie post-MMR chez les enfants indiens s'est avéré presque le double de celui des enfants non-indiens. Les enfants indiens qui étaient malades avant l'immunisation avaient plus de chances de'être malades au cours de la période de trois semaines post-MMR. Aucune relation semblable n'a été notée chez les enfants non-indiens. Ce résultats suggèrent que les enfants ayant une histoire de maladie frequente ont plus de chances d'être malades après le vaccin MMR. Ces résultats devront être confirmé par une étude de type prospectif.

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RUBELLA IMMUNIZATION policies in Canada generally advocate that children be given the vaccine, usually a combination measles-mumps-rubella, at age 12 months or older.[1] In Ontario, most infants are immunized at 15 months.[2] The vaccine can produce a fever, with or without a rash in some children. Other adverse reactions are extremely rare.

The prevailing clinical impression at Southwest Middlesex Health Centre has been that Indian children frequently present with illness, particularly respiratory infections, in the three weeks following MMR immunization. In an earlier study of morbidity among children living in southwestern Ontario, the incidence of office-reported illness during the first year of life in Indians was almost twice the rate for non-Indians.[3] The quality of medical care available to both groups of children was similar, yet this difference persisted into the second year.[4] In addition, Indian children were heavier than non-Indian children by the end of the first year; over 17% of the Indian infants were at or above the 95th percentile weight for sex compared to 4.4% of non-Indian infants.[5]

Our objective, therefore, was to determine whether or not the clinical impression was correct. Was the frequency of illness following MMR immunization greater among Indian children? If so, does this higher rate of illness merely reflect the ethnic difference in morbidity previously documented, or is there sufficient evidence to suggest that adverse reactions to MMR vaccine are more common in Indian children?

Southwest Middlesex Health Centre is a family practice located in a rural area approximately 25 km from London, Ontario. It is one of four family medical centres affiliated with the Department of Family Medicine at the University of Western Ontario. There are 4500 registered active patients, of whom one-third are Indians (Oneida, Chippewa, and Muncey bands) living on nearby reserves. The remaining two-thirds of the patient population are

Caucasian residents of neighboring rural communities.

Subjects and Methods

Southwest Middlesex Health Centre maintains a computerized age-sex register of active patients. By definition, patients are considered active if at least one household member visited the centre in the past two years. A listing of all children whose mothers were active patients of the centre at the time of delivery was obtained for the years 1974-1981. The following information was abstracted from the medical record for each child: sex, birthdate, gestational age, birthweight, ethnic origin (Indian or non-Indian), total number of visits to the health centre during the first 12 months of life, weight at 12 months, episodes of illness three weeks before and three weeks after MMR immunization was given (including after-hour visits), and date of MMR immunization.

We defined an episode of illness as all visits for a specific illness from its onset to its resolution.[6] If more than one visit was required for treatment, this was still regarded as a single episode.[4] Illnesses were coded according to the International Classification of Health Problems in Primary Care.[7] We excluded from consideration all diagnostic categories which could not possibly be related to MMR immunization i.e., injuries and trauma. The remaining categories were grouped as follows: upper respiratory infection, lower respiratory illness, otitis media, infective disease, skin disease, and fever.

During the years under study, the type of MMR vaccine used at the centre was changed. To examine the possibility that illness following MMR immunization might be related to the type of vaccine used, we also noted whether each child had received MMR ($HPV_{77}DE_5$) or MMR II (RA 27/3) vaccine.

We used the National Center for Health Statistics Growth Standards[8] as the basis for dividing children into obese and non-obese groups. Obesity was defined as weight at or exceeding the 95th percentile at age 12 months. The lower limits of obesity were 11990 grams for males, 11240 grams for females.

Standard statistical techniques were used to analyze the data, including the chi-square test for comparing two proportions in independent samples[9] and

the McNemar test to compare proportions in paired samples.[10]

Results

There were 146 Indian and 84 non-Indian children eligible for inclusion in the study. Of these, 19 (13%) Indian and three (3.7%) non-Indian children had been given the MMR vaccine after 24 months of age. We confined our analysis to children immunized between 11 and 24 months (127 Indian and 81 non-Indian).

Study cohorts

Males comprised 49.2% of the Indian cohort and 49.4% of the non-Indian cohort ($\chi_1^2 = 0.0$; $p>.05$). There was no ethnic difference in gestational age, birthweight, or frequency of attendance during the first year (Table 1). The mean age for MMR immunization was 15 months for Indians and 14 months for non-Indians. At age 12 months, Indian children were heavier and the proportion at or exceeding the 95th percentile was twice that of non-Indian children.

Type of vaccine

A slightly higher proportion of Indian children (66.1%) received $HPV_{77}DE_5$ vaccine compared to non-Indian children (54.3%) ($\chi_1^2 = 2.44$; $p=.12$).

In Indian children 20.2% (17 of 84) receiving $HPV_{77}DE_5$ vaccine and 16.3% (seven of 43) receiving RA 27/3 vaccine were ill at least once in the three weeks following immunization ($\chi_1^2 = 0.09$; $p>.05$). There was also no difference in the frequency of illness between the two types of vaccines in non-Indian children: 15.9% (seven of 44) of those given $HPV_{77}DE_5$ vaccine and 10.8% of the children given RA 27/3 vaccine had at least one episode of illness in the three weeks following immunization ($\chi_1^2 = 0.17$; $p>.05$).

Illness pre- and post-MMR

We examined the possibility that illness during the three weeks before the MMR vaccine was given might increase the risk of illness after immunization. In the Indian cohort, 23.8% of the children who were ill before immunization suffered an illness after the vaccine was given. Of the Indian children not ill pre-MMR, 16.5% were ill in the three weeks post-MMR (Table 2). No association between health status pre- and post-MMR was found for non-Indian children.

Although the difference between the two cohorts in the proportions receiving $HPV_{77}DE_5$ vaccine was not statistically significant, we looked at the relationship of health status before immunization to health status after immunization, according to the type of vaccine administered, to ensure that the relationship we observed in Indian children for illness pre- and post-MMR was not specific for the vaccine. Unfortunately, once the type of vaccine was taken into consideration, the number of children who were ill post-MMR was very small. Nonetheless, when the findings of 23.8% and 16.5% in Table 2 are separated according to the type of vaccine, the corresponding percentages are as follows: for $HPV_{77}DE_5$ vaccine, 27.3% and 17.7%; for RA 27/3 vaccine, 20.0% and 13.0%. Thus, although statistical techniques were not used because of small numbers, the relationship seemed consistent for both vaccines.

There was no association between weight at age 12 months and illness during the three weeks post-MMR in either cohort (Table 3). Therefore weight was not likely to influence the relationship shown in Table 2.

TABLE 1 Descriptive Characteristics of the Study Children

Characteristic	Indian (N=127) mean SE	Non-Indian (N=81) mean SE	t-value
Birthweight (g)	3378 (±58.5)	3292 (±74.8)	0.90
Gestational age (weeks)	39.6 (±0.2)	39.4 (±0.2)	0.40
Age at MMR (months)	15.4 (±0.3)	14.3(±0.2)	2.60; p=0.02
Weight at age 12 months (g)	10301 (±151.4)	9814 (±204.7)	1.95; p=0.06
Frequency of attendance (visits)	12.1 (±0.43)	11.8 (±0.58)	0.45

Illness following MMR immunization

The categories of illnesses which presented during the three weeks following immunization are shown in Table 4. The overall illness ratio of Indian to non-Indian children is 1.8.

Discussion

Indian children had a higher rate of office-reported illness during the three weeks after MMR immunization compared to non-Indians (Table 4). The difference in illness rates is almost identical to the difference (or ratio) found in comparisons of annual rates reported previously. The risk of illness in Indian children relative to non-Indian children has been 1.8 in the first year[3] and 1.5 in the second year.[4] Thus, the overall rates of illness are as expected.

The incidence of otitis media and lower respiratory disease among Indian children in previous reports is very high; our findings agree with these earlier reports.[3, 4, 11, 12]

Once the health status post-MMR was examined in relation to health status pre-MMR, however, there was an indication that some children may be at greater risk of illness following immunization. We found that Indian children who visited with an illness before immunization were more likely to be seen with an illness in the post-MMR period.

The ethnic difference in age at immunization was statistically significant. This difference, however, is not clinically significant, because the mean ages were only one month apart and well within the guidelines suggested by present immunization policies.[1, 2]

We included weight at age 12 months as a variable because we suspected that Indians in this study may be heavier, and we did not know if this would increase the risk of illness after immunization. The increased frequency of illness in Indian children post-MMR was not, in fact, associated with weight at age 12 months.

Indian children have been found to attend fewer well baby examinations during the first year than non-Indian children.[3] Thus, the lack of a difference in the number of visits to the health centre suggests that while Indians are ill more often than non-Indians, the overall use of the medical facility is similar.

The National Advisory Committee on Immunization has stated that "minor infections, such as the common cold, are very common in pediatric age groups and are not contraindications to immunization".[1] Our study, based on office-reported illness, seems to indicate that children with an established record of frequent illness, as is the case for many Canadian Indian children, are likely to experience an illness following MMR immunization. If this finding is confirmed by prospective studies assessing complete morbidity, rather than a chart review, it may be desirable to modify current recommendations. Immunization could be delayed, within reasonable time limits, until the high-risk child has experienced three illness-free weeks.

TABLE 2
Illness Pre- and Post-MMR in Indian and non-Indian Children

Post-MMR	Not ill No.	Not ill (%)	Ill No.	Ill (%)
Indian Pre-MMR				
ill	14	(16.5)	10	(23.8)
not ill	71	(83.5)	32	(76.2)
	85	(100.0)	42	(100.0)
McNemar χ^2 = 6.28 (p=.012)				
Non-Indian Pre-MMR				
ill	9	(13.2)	2	(15.4)
not ill	59	(86.8)	11	(84.6)
	68	(100.0)	13	(100.0)
McNemar χ^2 = 0.05 (p=.83)				

TABLE 3
Weight at Age 12 Months and Illness Following MMR Immunization

Percentile weight	Not ill No.	Not ill (%)	Ill No.	Ill (%)
Indian				
<95th	75	(84.3)	15	(78.9)
≥95th	14	(15.7)	4	(21.1)
	89	(100.0)	19	(100.0)
χ^2_1 = 0.05 (p=.82)				
Non-Indian				
<95th	54	(93.1)	8	(88.9)
≥95th	4	(6.9)	1	(11.1)
	58	(100.0)	9	(100.0)
χ^2_1 = 0.00 (p=1.0)				

TABLE 4
Rate* of Episodes of Illness During the 21 days Post-MMR

Diagnostic category	Indian (N=127)	Non-Indian (N=81)
Upper respiratory infection	5.5	3.7
Lower respiratory infection	5.5	0
Otitis media	7.9	2.5
Infective disease	0.8	4.9
Skin disease	4.7	2.5
Fever	1.6	1.2
Total	**26.0**	**14.8**

* $\frac{\text{No. of episodes}}{\text{No. of children at risk}} \times 100$

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